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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/032,108	12/20/2001	Timothy David Osslund	01017/38834F	7916
7590 Marshall Gerstein & Borun LLP 6300 Sears Tower 233 South Wacker Drive Chicago, IL 60606			EXAMINER LUCAS, ZACHARIAH	
			ART UNIT 1648	PAPER NUMBER
			MAIL DATE 06/08/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/032,108	Applicant(s) OSSLUND, TIMOTHY DAVID	
	Examiner Zachariah Lucas	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 March 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 62,66,75,76,79 and 81-83 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 62,66,75,76,79 and 81-83 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Currently, claims 62, 66, 75, 76, 79, and 81-83 are pending and under consideration.
2. In the prior action, mailed on October 17, 2006, claims 62, 66, 75, 76, 79, and 81-83 were pending and rejected.

In the amendment of March 23, 2007, the Applicant amended claims 75 and 76.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. **(Prior Rejection- Maintained)** Claims 62, 66, and 81-83 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are drawn to modified G-CSF molecules comprising a substitution in "an external loop." The claims were rejected because it is not clear what residues form the referenced external loops. In view of the Applicant's assertion that the determination of the helices and the loops is subjective in nature, the rejection is extended to claims 75, 76, and 79, which also require modifications in undefined (according to Applicant's arguments) helical regions.

The Applicant traverses the rejection on the basis that the identification of protein residues in helical versus loop regions is subjective, and that the teachings provided in the present application would enable those in the art to determine which modifications fall within the scope of the claims. This argument is not found persuasive. The Applicant is essentially asserting

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that the scope of the claims varies according to the party who is attempting to practice the claimed invention based on the disclosure, and that it is irrelevant that different parties may make different determinations as to what modifications fall within the scope of the claims. This argument is not found persuasive. 35 U.S.C. 112, second paragraph requires that the claims clearly define the metes and bound of the claimed invention. MPEP 2173.05(a). In particular, the MPEP states that this statute requires that the claims provide “clear warning to others as to what constitutes infringement of the patent” (MPEP 2173.02), and that they provide “clear measure of what applicants regard as the invention” (MPEP 2173). In this case, because of the uncertainty as to what residues the Applicant considered to be in what regions of the protein (and thus as to what modifications the Applicant considers to fall within the scope of the claims), and because, by Applicant’s own admission, different parties would come to different conclusions as to what modifications would and would not fall within the scope of the claims, the rejection is maintained.

Claim Rejections - 35 USC § 102 and 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. **(Prior Rejection- Withdrawn)** Claims 75, 76, and 81-83 were rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over

Shaw et al., U.S. 4,904,584. These claims have been amended to require amino acid substitutions in helix C of the G-CSF protein. This rejection is therefore withdrawn in favor of the rejections below.

7. **(Prior Rejection- Maintained)** Claims 62, 66, and 81-83 were rejected under 35 U.S.C. 103(a) as being unpatentable over Shaw (U.S. 4,904,584), and further in view of Bazan (Immunology Today 11: 350-54).

The Applicant asserts that there is no motivation for those of ordinary skill in the art to combine the teachings of Shaw and Bazan. The Applicant presents two arguments in support of this assertion.

First, the Applicant asserts that reliance on Bazan is inappropriate because the reference neither expressly nor implicitly suggests the limitations of the claims. In particular, the applicant asserts that if Bazan suggests any modifications to G-CSF, it is to the helical regions. This argument is not found persuasive. The motivation to combine is found in the teachings of Shaw, which indicates that those of ordinary skill in the art to look to teachings in the art for guidance as to what residues or regions of the indicated proteins, including G-CSF, would be suitable targets for modification such that a lysine could be inserted and a PEG attached thereto. Because Shaw provides such motivation for the combination, the Applicant's first argument is not found persuasive.

The Applicant next asserts that Bazan does not rule out the functional significance of the loop regions in that the reference points to a portion of one loop of a related protein that may be involved in the protein's function. Page 352. Nonetheless, the teachings of the reference indicate

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that the loop regions in general are appropriate targets for lysine modification, and provide sufficient information such that those of ordinary skill in the art would have a *reasonable expectation* of success in modifying the loop regions such that PEG molecules could be attached to lysines substituted therein. Moreover, while the Applicant points to specific guidance in the present application as to binding regions in the G-CSF molecule, it is noted that these regions generally conform to the teachings of the Bazan in that the binding regions are found in the helices. It is noted that even residues 11-57, which comprises some residues in the G-CSF loop regions, is described by the Applicant as comprising residues "between the A and AB helix." Response, page 11. Thus, while the teachings of the present application are not identical to the teachings in Bazan, those of ordinary skill in the art would nonetheless have had a reasonable expectation of success in the combination of Shaw and Bazan for the making of operable G-CSF PEGylated variants.

The rejection is therefore maintained for the reasons above, and the reasons of record.

8. **(Prior Rejection- Maintained)** Claims 62, 66, 75, 76, 79, and 81-83 were rejected under 35 U.S.C. 103(a) as being unpatentable over either Shaw, or Shaw in view of Bazan as applied, respectively, against claims 75, 76, and 81-83, or claims 62, 66, and 81-83 above, further in view of Bowie (Science 247:1306-1310). In view of the amendment of claims 75 and 76, the rejection is restated as a rejection of claims 62, 66, 75, 76, 79, and 81-83 under 35 U.S.C. 103(a) as being unpatentable over Shaw in view of Bazan, and further in view of Bowie.

The Applicant traverses this rejection for substantially the same reasons as indicated above, and on the basis that the Bowie reference does not provide any specific teachings

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regarding the modification of G-CSF. The arguments with respect to the combination of Shaw and Bazan are not found persuasive for the reasons indicated above. The arguments regarding the additional teachings of Bowie are also not found persuasive. The teachings of this reference indicate that those of ordinary skill in the art would have a reasonable expectation that modifications could be made to proteins without a loss of function. Because the teachings of Bazan indicate the structure of the G-CSF molecule, it would have been obvious to those of ordinary skill in the art to make minor (e.g. conservative) mutations to the helical regions. Other teachings in the art indicate that those in the art would have had additional motivation to modify such regions. See e.g., the teachings of O'Shea (Science, 254:539-544, esp. pages 541 and 543), and Tsuji et al. (Proteins, 9:12-22, esp. page 13, right column) (each indicating that those of ordinary skill in the art were aware that modifications to residues in helical domains of proteins could be used to stabilize protein conformational structure, and thus would be motivated to make such modifications). However, as the present claims do not ascribe any particular function to the modifications, and as the teachings of Bowie indicate that the making of modifications to proteins was generally tolerated without a loss of function, the present claims fail to identify a non-obvious variant of G-CSF.

The rejection is therefore maintained for the reasons above, and the reasons of record.

Conclusion

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Z. Lucas/

Patent Examiner, AU 1648